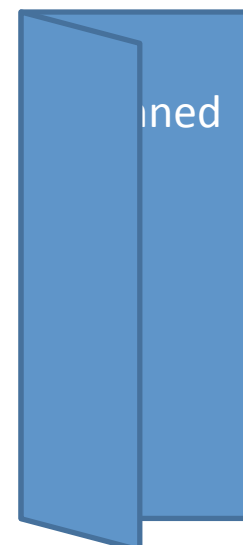


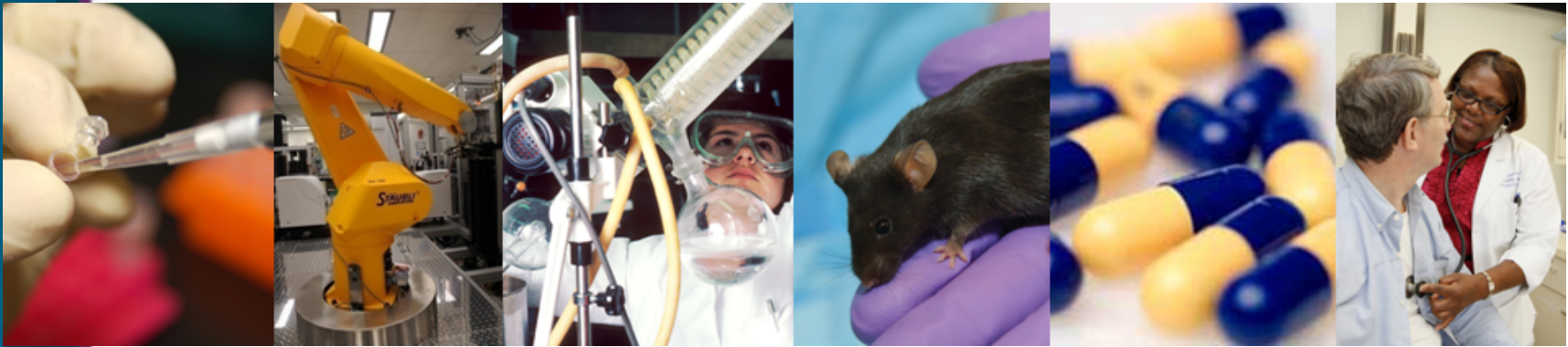
"C'mon, c'mon—it's either one or the other."



NCATS: NIH Center for Advancing Translational Sciences, Overview

Noel Southall, PhD
Informatics, NIH/NCATS
February 4, 2013

NCATS Mission



To catalyze the generation of innovative methods and technologies that will enhance the development, testing and implementation of diagnostics and therapeutics across a wide range of human diseases and conditions.

Characteristics of NCATS Initiatives and Programs

- Address significant bottlenecks in the process of translation
- Highly collaborative across NIH, other government agencies, and with the private sector.
- Quick to respond to needs of biomedical researchers

NCATS Informatics

- Experimental design, data analysis and software development in support of research projects:
 - » Laboratory information management
 - » High-throughput screening data analysis
 - » RNAi screening data analysis
 - » Bioinformatics support
 - » Ligand-based modeling support
 - » Structure-based modeling support
 - » Statistics support
 - » Web application development
 - » Computational tool development



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Links

- NCATS
- NCGC
- NHGRI
- PubChem

Presentations

- ACS Spring 2010
- Chemaxon UGM 2008
- Chemaxon UGM 2011
- Chemaxon UGM 2012

Software

- Automated R-group analysis
- Fragment activity profiler
- Kinome navigator
- Kinome viewer
- Library synthesizer
- Molecular framework
- MolPlot
- MolSubspace
- Multiple MCS
- PubChem search server
- Scaffold activity diagram
- Siphonify
- Structure standardizer
- Tautomer generator
- The NPC browser
- Tox21 chemical browser

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About



tripod

What's in the name. The name **Tripod** can be thought of as an acronym for Therapeutically Relevant Informatics for Prioritization, Optimization, and Development. It also symbolically represents a support structure—which consists of biology, chemistry, and informatics—for a typical therapeutic project.

Contributors are members of the informatics group within the [Division of Preclinical Innovation, National Center for Advancing Translational Sciences](#). If you have any questions regarding Tripod postings or resources, please contact [Ajit Jadhav](#).

NCATS' Therapeutics for Rare and Neglected Diseases (TRND)

- Preclinical development expertise applied to rare disease programs
- To what extent should NCATS' portfolio invest in drug repurposing approaches for rare diseases?
 - » How successful had it been historically?
 - » Were there existing programs that were stalled?
 - » Best methods for generating repurposing leads?
- Collaborate with FDA/OOPD - Office of Orphan Products Development
 - » Rare disease repurposing database (RDRD)
 - » Orphan product designation coupled to UNII generation

FDA Substance Registration System

Food and Drug Administration Substance Registration System Standard Operating Procedure

Title: Substance Definition Manual ¹	Version: 5c
Effective Date: June 10, 2007	Supersedes: Version 5b
Approved By: SRS Chemistry Review Committee; FDA Data Standards Council's Vocabulary	

 U.S. Department of Health & Human Services

 **U.S. Food and Drug Administration**
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For Industry

[Home](#) [For Industry](#) [Data Standards](#) [Substance Registration System - Unique Ingredient Identifier \(UNII\)](#)

Data Standards

- ▶ **Substance Registration System - Unique Ingredient Identifier (UNII)**
- Substance Registration System – UNII Presentation

Substance Registration System - Unique Ingredient Identifier (UNII)

The overall purpose of the joint FDA/USP Substance Registration System (SRS) is to support health information technology initiatives by generating unique ingredient identifiers (UNIs) for substances in drugs, biologics, foods, and devices. The UNII is a non-proprietary, free, unique, unambiguous, non-semantic, alphanumeric identifier based on a substance's molecular structure and/or descriptive information.

The procedures and management of the SRS is provided by the SRS Board. The SRS Board includes experts from both FDA and USP. The SRS operating procedures defined by the SRS Board are detailed in the SRS Manual.

The UNII is:

- One of the core components of the United States Federal Medication Terminology.
- Used in the FDA's Structured Product Labeling
- Used to assist in the generation of the National Library of Medicine's (NLM's) RxNorm.
- A US government standard for drug ingredient and food allergen identifiers
- A component of the Environmental Protection Agency's Substance Registry System (future)

The UNII may be found in:

- NLM's Unified Medical Language System (UMLS)
- National Cancer Institutes Enterprise Vocabulary Service
- USP Dictionary of USAN and International Drug Names (future)
- FDA Data Standards Council website
- VA National Drug File Reference Terminology (NDF-RT)
- FDA Inactive Ingredient Query Application

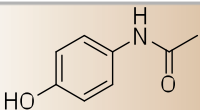

Questions about the UNII should be directed to fda-srs@fda.hhs.gov

NCATS' Therapeutics for Rare and Neglected Diseases (TRND)

Drug registration information informing program policy, strategy

- How successful had it been historically?
 - » Surprisingly successful (e.g. CF)
 - » Not always straight-forward (lenalidomide)
- Were there existing programs that were stalled?
 - » Generally not for business reasons
- Best methods for generating repurposing leads?
 - » Random screening approaches complement directed ones
- How to build a physical library for repurposing screens?

How Many Drugs Are There?

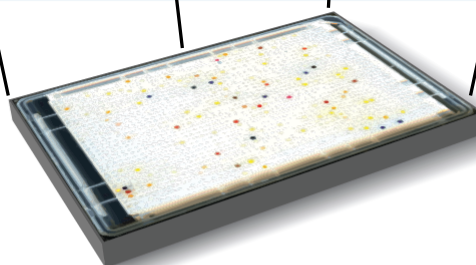
	Term	FDA	Worldwide	
Tylenol 8 Hour, Dayquil Sinus NyQuil Cough, Infants' Tylenol	Drug Product	>140,000		Product with defined package size, dose, formulation of API(s)
Tylenol, Acetaminophen, Panadol, Datril, Paracetamol	Drug	>19,000	>25,000	Brand or generic name of approved product that defines API(s)
103-90-2	API	4,695	7,980	Physical substance intended to be used in manufacture of drug product
	Active Moiety	2,794	4,374	Chemical moiety excluding salts, esters, etc. responsible for pharmacological activity
	HTS Suitable	1,817	2,750	Chemical entity of defined structure amenable to high-throughput screening

Informatics sources for NPC

- US FDA: Orange Book, OTC, NDC, Green Book, Drugs@FDA
- Britain NHS
- EMA
- Health Canada
- Japan NHI

Physical sources for NPC

- Procurement from >70 suppliers worldwide
- In-house purification of APIs from marketed forms
- Custom synthesis



Registration of Substances and Related Information Based on ISO 11238

Scope

This International Standard provides an information model to define and identify substances within medicinal products or substances used for medicinal purposes, including dietary supplements, foods and cosmetics.

INTERNATIONAL
STANDARD

ISO
11238

First edition
2012-xx-xx

Health informatics — Identification of medicinal products — Data elements and structures for the unique identification and exchange of regulated information on substances

Informatique de santé — Identification des médicaments — Éléments de données et structures pour l'identification unique et l'échange d'informations réglementées concernant les substances



Reference number
ISO 11238:2012(E)

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A Path to ISO 11238 Implementation

- FDA/OC considering update of SRS to ISO 11238 standard
- NCATS motivated by interest, experience and aligned mission
- HHS Interagency Research Collaboration Agreement to structure the collaboration



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ISO 11238 Implementation

- Enable the deposition of new substances and relationships between substances
- Adhere to the ISO standard for each type, grouping of substance
- Provide a reference for every annotation within the system
- Publish/distribute public information on substance registrations
- Cooperate on depositing substances into a 'master' system that can issue ISO IDs



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Man v Software; e.g. Uniqueness

- The system must support the adjudication of substance records by a regulatory authority, not automate or replace that adjudication
 - » The capture of specified substances must satisfy existing regulations; e.g. EMA SPC and USC/CFR
 - » Be responsive to the needs of product sponsors and the innovation presented by new products
- Where possible, that framework ('business rules') should be tested algorithmically during substance entry to ensure consistency across registrations
 - » Ultimate responsibility rests with a registrar, however
 - » Relevant (defining) aspects of that decision should be captured

Meeting Goals

- Encourage international cooperation on the implementation of ISO 11238
- Discuss the practicalities of implementing the standard for each of the different types of specified substances
- Identify additional functional requirements for an implementation system



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